rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Regarding submission of copyright form for book chapter

2 messages

Ram Sahu <ramsahu79@gmail.com> Sat, Mar 6, 2021 at 6:35 PM
To: rr retno widyowati <rr-retno-w@ff.unair.ac.id>, retno widyowati <retno_biotek@yahoo.com>, Andang MIATMOKO <andang-m@ff.unair.ac.id>

Dear Authors,

We would like to let you know that your book chapter has been sent to Bentham Science Publisher for the forthcoming book **"Advanced Pharmaceutical and Herbal Nanoscience For Targeted Drug Delivery Systems".** The Principal author must submit a copyright form for their book chapter for further processing of book.

Please return the copyright form attached to this email by filling out all of the information requested by the publisher. For your convenience, I've added book chapter.

Looking forward for your prompt response.

Please feel free to contact me in case of any confusion.

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA
09893577279

3 attachments

Copyright Form_Author.pdf
287K

4 Dr Retno Widyowati.docx
928K

24 Dr Andang.docx
1031K

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Sun, Mar 7, 2021 at 2:42 PM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr. Ram Sahu,

Herewith I send back the author copy and also revise the coauthor in my chapter.

Thank you and best regards,

Retno Widyowati, PhD
Department of Pharmaceutical Sciences
Faculty of Pharmacy, Universitas Airlangga

[Quoted text hidden]

2 attachments

Book Chapter-Phytoconstituents.docx
1057K

Copyright Form_Author copy.pdf
626K

rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Figure Improvement Query for Book Chapter | BMS-APHNT-2021-HT1-2938-1

3 messages

Ram Sahu <ramsahu79@gmail.com> Tue, May 4, 2021 at 12:01 PM
To: dalahora@ksu.edu.sa, aajayi22@lautech.edu.ng, "Dr. Sudarshan Singh" <sudarshansinghi10@gmail.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, rjanto@rgcb.res.in, Sunita M <sunita3481@gmail.com>, prashardeepak99@yahoo.in, subhashis.ooty@gmail.com, anupomborah@gmail.com, harsha1975@gmail.com, dr_santosh@msu.edu.my, emfaller@ceu.edu.ph, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, "jiyauddin_khan@msu.edu.my" <jiyauddin_khan@msu.edu.my>, Andang MIATMOKO <andang-m@ff.unair.ac.id>, pharm.anas.alhamdany@uomustansiriyah.edu.iq, sursrija0714@gmail.com

Dear Professors,

This is with reference to your chapter submitted for the proposed book entitled **"Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems "** submitted for possible publication in the Bentham Science Publisher.

Please find below the comments of the Editor for your necessary action. Kindly address the following comments and submit your revised chapter for further consideration.

During graphics assessment, it has been observed that the figure(s) no. **Chapter 01 Fig-2,3,4, Chapter 02 Fig-1,2 Chapter 03 Fig-1 Chapter 04 Fig-1,2 Chapter 05 Fig-1,2 Chapter 06 Fig-1 Chapter 08 Fig-1,2 Chapter 09 Fig-1 to 4 Chapter 10 Fig-1 to 4 Chapter 11 Fig-1,2 Chapter 12 Fig-1,2 Chapter 16 Fig-1 to 7 Chapter 17 Fig-1 to 7 Chapter 18 Fig-1,2 Chapter 19 Fig-1,2 Chapter 20 Fig-1,2 Chapter 22 Fig-1 to 5 Chapter 24 Fig-1 to 10 Chapter 25 Fig-1 Chapter 26 Fig-1 to 6** embedded in your article, have not been provided according to the recommended parameters **[please see attached technical details]**. For your reference, we have attached before and after figure improvement, sample images. Further **chapter number along with chapter title attached**, so authors are suggested to check their chapter number and make appropriate modification in figure.

It is, therefore, requested to have your figures improved.

Please note that no article will be published with substandard figures.

Please also note, that improved figures, alone, do not guarantee the final publication of your article. The final acceptance/rejection decision on the manuscript will be taken by the EIC, based on the quality of the article and independent peer review.

We would appreciate it if you could submit the revised chapter by May 8, 2021.

Feel free to contact for any queries.

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA
09893577279

2 attachments

List of Chapter number.pdf
70K

95675_lab_report.pdf
687K

---

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Sun, May 9, 2021 at 6:18 PM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr. Ram Sahu,

Herewith I send Figures 1 and 2 for Chapter 4.
Hope they are ok

Best Regards,

Retno Widyowati, PhD
[Quoted text hidden]

2 attachments

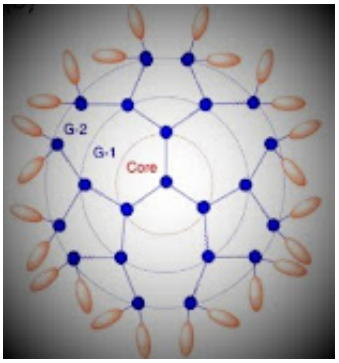

figure 2 Cap 4600 (1).jpg
30K

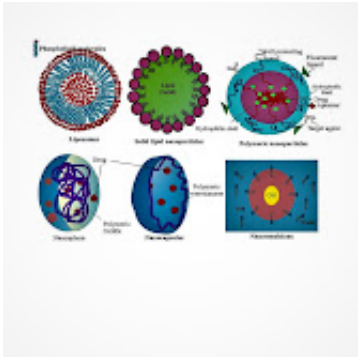

Figure 1 Cap 4600 (2).jpg
185K

Ram Sahu <ramsahu79@gmail.com> Sun, May 9, 2021 at 7:22 PM
To: rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Dear Professor,
Figure 1 is ok, but the FIgure 2 is still blurry and it needs modifications.....
[Quoted text hidden]

rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Figure Improvement Query for Book Chapter | BMS-APHNT-2021-HT1-2938-1

1 message

Ram Sahu <ramsahu79@gmail.com> Mon, Jul 5, 2021 at 8:14 AM
To: rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, Sunita M <sunita3481@gmail.com>, ERWIN FALLER <erwinfaller1007@gmail.com>, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, Andang MIATMOKO <andang-m@ff.unair.ac.id>

Dear Professors,

This is with reference to your chapter submitted for the proposed book entitled **"Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems "** submitted for possible publication in the Bentham Science Publisher.

Please find below the comments of the Editor for your necessary action. Kindly address the following comments and submit modified figure for further consideration:

Thank you for providing us improved figures for your manuscript entitled, **"Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems "**, submitted for possible publication in the book **"Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems"**. I would like to inform you that the provided improved figure(s) number of **Chapter 04 Fig-1,2; Chapter 05 Fig-1,2; Chapter 08 Fig-1,2; Chapter 17 Fig-1 to 7; Chapter 18 Fig-1,2; Chapter 19 Fig-1,2; Chapter 22 Fig-1,3,4,5 and Chapter 24 Fig-1 to 10** being blurry and distorted, still cannot be proceeded for publication in the present form.

Therefore, you are requested to send the source file of the figure(s). And, the figure(s) must be prepared according to the following instructions.

Requirement
Width = 8.5 inches OR Width= 7791px (In-between)
Height = 11 inches OR Height = 4724px (In-between)
Pixels/Centimeter = 300 (DPI) (minimum)
All figure should be in vector scale

It is, therefore, requested to have your figures improved.

We would appreciate it if you could submit the figure by July 8, 2021.

Feel free to contact for any queries.

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA
09893577279

rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Comments of reviewers for Book Chapter

5 messages

Ram Sahu <ramsahu79@gmail.com> Wed, Sep 8, 2021 at 12:16 PM
To: Doaa Al-Ahora <dalahora@ksu.edu.sa>, Ayodeji Ajayi <aajayi22@lautech.edu.ng>, "Dr. Sudarshan Singh" <sudarshansinghi10@gmail.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, "Dr.Ruby John Anto" <rjanto@rgcb.res.in>, sharmadibru@gmail.com, Sunita M <sunita3481@gmail.com>, prashardeepak99@yahoo.in, subhashis.ooty@gmail.com, anupomborah@gmail.com, harsha1975@gmail.com, vishal trivedi <vishaltrivediqa@gmail.com>, "SH. VINOD NAUTIYAL" <vnautiyal@gkv.ac.in>, raousm@gmail.com, raousm@unisza.edu.my, dr_santosh@msu.edu.my, ERWIN FALLER <erwinfaller1007@gmail.com>, emfaller@ceu.edu.ph, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, "jiyauddin_khan@msu.edu.my" <jiyauddin_khan@msu.edu.my>, uditaagrawal.phama@gmail.com, Andang MIATMOKO <andang-m@ff.unair.ac.id>, pharm.anas.alhamdany@uomustansiriyah.edu.iq, SRIJA SUR <sursrija0714@gmail.com>, vivek dave <attachvivek@gmail.com>

Dear Authors,

Greetings

We hope you and your family stay healthy during the Pandemic.

We received comments from reviewers on book chapters of the book **"Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems".** According to the comments of reviewers, the author should have their book chapter verified by a native English expert and attach a certificate of the same.

Listed below is the editor's message:

"Thanks for submitting the manuscript to **"Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems".** Your book chapters has been reviewed by experts in the field, and it needs substantial revision (comments given below/ attached). You are encouraged to carefully revise the manuscript, highlighting the exact changes made.
Our publication policy requires the return of your revised manuscript latest within one weeks of the receipt of this message.

Reviewer Comments:

Comment No. 1:

The book is well written and it is very easy to read. I believe that it can attract the readers of nanoscience and nanotechnology, more especially those specializing in drug delivery. Nonetheless, before it could be considered for publication, a few points need to be addressed. **• The quality of the images needs to be improved, otherwise the current images degrades the quality of the chapters. • Some of the used images were adopted from the journals or other internet search engines, I will**

strongly request that authors reference those journals or internet sides. Basically, most of the chapters in this book do contain images adopted from other sources. The grammar needs to be improved significantly, and recommended for the correction by a native English speaker. The certificate of native English expert must be attached.

Comment No. 2:

The reviewer recommends this book for publication."

Expecting to get the revised book chapter before the deadline, and please contact me if you have any questions.

Regards,

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA
09893577279

Erwin M. Faller <emfaller@ceu.edu.ph> Wed, Sep 8, 2021 at 10:21 PM
To: Ram Sahu <ramsahu79@gmail.com>
Cc: Doaa Al-Ahora <dalahora@ksu.edu.sa>, Ayodeji Ajayi <aajayi22@lautech.edu.ng>, "Dr. Sudarshan Singh" <sudarshansinghi10@gmail.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, "Dr.Ruby John Anto" <rjanto@rgcb.res.in>, sharmadibru@gmail.com, Sunita M <sunita3481@gmail.com>, prashardeepak99@yahoo.in, subhashis.ooty@gmail.com, anupomborah@gmail.com, harsha1975@gmail.com, vishal trivedi <vishaltrivediqa@gmail.com>, "SH. VINOD NAUTIYAL" <vnautiyal@gkv.ac.in>, raousm@gmail.com, raousm@unisza.edu.my, dr_santosh@msu.edu.my, ERWIN FALLER <erwinfaller1007@gmail.com>, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, "jiyauddin_khan@msu.edu.my" <jiyauddin_khan@msu.edu.my>, uditaagrawal.phama@gmail.com, Andang MIATMOKO <andang-m@ff.unair.ac.id>, pharm.anas.alhamdany@uomustansiriyah.edu.iq, SRIJA SUR <sursrija0714@gmail.com>, vivek dave <attachvivek@gmail.com>

This a great news that our book will be published soon (ofcourse some technicalities need to be addressed).

Congratulations to all..

Regards,

Erwin
[Quoted text hidden]

---

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Wed, Sep 15, 2021 at 7:46 AM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr. Ram

Here is I send the revision of the book chapter that I did for proofreading.
Good luck

Best regards,

Retno Widyowati, PhD

[Quoted text hidden]

Chapter IV-phytoconstituents.docx
1097K

---

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Wed, Sep 15, 2021 at 7:56 AM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr Ram,

I am so sorry .... this is the correct one

Best Regards,

Retno Widyowati, PhD

[Quoted text hidden]

Chapter IV-phytoconstituents.docx
1102K

Ram Sahu <ramsahu79@gmail.com> Wed, Sep 15, 2021 at 8:35 AM
To: rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Thanks a lot Professor
[Quoted text hidden]

rr retno widyowati <rr-retno-w@ff.unair.ac.id>

(no subject)

3 messages

Ram Sahu <ramsahu79@gmail.com> Wed, Dec 15, 2021 at 7:41 PM
To: retno widyowati <retno_biotek@yahoo.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Dear Professor Retno,
Kindly find the attachment of the chapter on which editing is required.
The comment of the publisher is given below:
"Therefore, it is requested that you get all the grammatical and scientific inconsistencies present throughout the book corrected by a **professional Scientific Content Editor** and submit a thoroughly edited and revised version along with a certificate of editing to qualify for further processing of the article."
Kindly make modification accordingly

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA
09893577279

4 Dr Retno Widyowati.docx
393K

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Fri, Dec 24, 2021 at 6:34 AM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr. Ram,

Here is I send the proofreading results and certificate from professional proofread.

Thank you very much.

Best regards,

Retno Widyowati, PhD
[Quoted text hidden]

2 attachments

4 Dr Retno Widyowati-proofread.docx
422K

Certificate of Proofreading Retno Widyowati et al. 23-12-21.pdf
428K

Ram Sahu <ramsahu79@gmail.com> Fri, Dec 24, 2021 at 6:47 AM

To: rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Thank you very much Professor
[Quoted text hidden]

CHAPTER 4

Pharmaceutical Nanosciences and Their Application for the Delivery of Different Phytoconstituents

Retno Widyowati[1,2]*, Andang Miatmoko[1]

[1]Department of Pharmaceutical Science, Faculty of Pharmacy, Universitas Airlangga, Surabaya, 60115, Indonesia

[2]Natural Product Drug Discovery and Development Research Group, Faculty of Pharmacy, Universitas Airlangga, Surabaya, 60115, Indonesia

*Corresponding Author: rr-retno-w@ff.unair.ac.id

ABSTRACT

Nanoscience provides many opportunities for pharmaceutical scientists. Throughout the developing progress of nanoparticle-based medicine preparations, the opportunity to overcome and treat difficult diseases, especially in herbal medicine, can be provided. The use of herbs is effective when the active constituents reach the target. Flavonoids, tannins, and terpenoids in herbs are hydrophilic and unable to pass through cell lipid membranes, therefore, their absorption is poor, resulting in reduced availability and biological efficacy, increased dosage and frequency of use. Nanoengineering has verified that nanoparticles have great prospects as drug carriers. The size reduction methods and technologies produce a wide variety of nanostructures that indicate particular physicochemical and biological properties. This delivery system has an essential function in increasing the solubility, bioavailability, pharmacological, steadiness, effectiveness, selectivity, and drug specificity of the bioactive constituents. Nanoscale models like phytosomes, liposomes, nanoemulsions, nanoparticles, solid lipid nanoparticles, and ethosomes are used to deliver different bioactive constituents at adequate doses to the target and throughout the entire treatment period. Recently, phospholipid complex techniques have been introduced to overcome these barriers either by increasing their dissolving capacity or their potential ability to pass through biological membranes and also protecting the active herbal constituents from degradation. Therefore, this chapter will discuss the application of nanoscience and its application in delivering different phytoconstituents to achieve therapeutic targets.

Hira Jamshaid 13/12/21 10.01
Deleted: work

Hira Jamshaid 13/12/21 10.01
Deleted: ,

Hira Jamshaid 13/12/21 10.01
Deleted: ,

Hira Jamshaid 13/12/21 10.02
Deleted: work

Keywords: Nanotechnology, herbal medicine, phytoconstituents

INTRODUCTION

Nanotechnology is a science that manipulates the dimensions of matter at nanoscale. Recently, this science has been needed for the pharmaceutical and drug industries because it is promising and has a crucial function in improving the life of mankind. The applications used in this science are related to the medical field, such as the therapeutic application of drug delivery, enhancing drug efficacy, reducing side effects, and improving circulation and stability [1]. Most of the phytoconstituents are declared active if they are evidenced to have definite impacts on treating definite diseases or relieving ache and are classified as organic constituents. Mostly, the active organic constituents are non-water soluble, have low bioavailability, are unstable, and are the most toxic.

Nanoparticles are often used for therapeutic and diagnostic agents because of their advanced and urgently needed drug delivery systems. For example, materials incorporating protein or nucleic acids need a carrier system that may increase their effectiveness and shield them from undesired decreation [2]. The potency of the drug nanoparticle delivery system is straightly associated with its small particle and huge surface area, thus indicating increased solubility and the capability to pass through the blood-brain barrier (BBB), enter the respiratory organ system, and be captived across the close connections of skin epithelial tissue cells [3].

Formulations using herbal medicines or their active phytoconstituents still face many limitations [4]; however, these medicines are a major source because of their lower side effects compared to synthetic drugs and deep-rooted public belief to cure or prevent various diseases. To overcome these limitations, several methods are used, such as dissolving in non-polar solvents, making injection preparations, and increasing the solubility by changing the active phytoconstituents into their salt form. These methods have several drawbacks, such as high solvent toxicity, their activity in the form of salt that is not clear, the presence of bioactive forms of drugs, and the lack of bioavailability, therefore, special technology is needed, namely nanotechnology as a solution. With nanotechnology, herbal medicines can deliver their active phytoconstituents to specific targets. These nanoparticle techniques are designed and provided in various sizes, forms, compositions, functions, and physical/chemical modifications to suit the distinctiveness of the targeted organs and drug. The dosage forms of nanoparticles are fullerenes, emulsions,

Hira Jamshaid 13/12/21 10.02
Deleted: n

Hira Jamshaid 13/12/21 10.02
Deleted: a

Hira Jamshaid 13/12/21 10.03
Deleted: is

Hira Jamshaid 13/12/21 10.03
Formatted: Highlight

Hira Jamshaid 13/12/21 10.03
Deleted:

Hira Jamshaid 13/12/21 10.03
Deleted: -

Hira Jamshaid 13/12/21 10.04
Formatted: Highlight

Hira Jamshaid 13/12/21 10.04
Formatted: Highlight

Hira Jamshaid 13/12/21 10.05
Deleted:],

Hira Jamshaid 13/12/21 10.06
Formatted: Highlight

Hira Jamshaid 13/12/21 10.06
Deleted: so that

microemulsions, liposomes, liquid crystals, dendrimers, quantum dots, nanoparticles, gels, solid lipid nanoparticles, and others. Thus, this chapter will briefly focus on herbal medicines nanoparticles to solve several deficiencies in formulation associated with phytoconstituents in herbs.

PHYTOCONSTITUENTS IN HERBAL MEDICINE

Phytoconstituents found in herbs are commonly called secondary metabolites, namely phenolics, terpenoids, alkaloids, and anthraquinones. These compounds have high curative value, but their bioavailability and solubility are low, and their toxicity and stability may hinder their medicinal use [5].

Phenolic

Almost all plants contain phenolic compounds, which are aromatic compounds with more than one hydroxyl substituent. The main compounds are phenols and many are found in polyphenols, out of which more than 8000 compounds have been identified. Based on their primary chemical structures, polyphenols are divided into stilbenes, phenolic acids, flavonoids, and lignans. Flavonoids are one of the polyphenols obtained from nature; more than 6000 compounds have been identified. Flavonoid includes flavones, flavonols, flavans, flavanones, dihydroflavanols, isoflavons, and biflavones [6]. The compounds of this class have the function of protection against free radicals, cardiovascular, cancer, inflammation, microbial, viral, allergic, ulcer, and other diseases [7]. Other phenolic compounds are quinones, xanthones, coumarins, polymer lignins, and tannins. Phenylpropanoid dimers or lignans containing two C6-C3 bound by C-8 carbon centres have antivirus, anticancer, anti-inflammatory, antimicrobial, antioxidant, immunosuppressive, and hepatoprotective activities, and are used for osteoporosis prevention [8].

Polyphenols have properties that are difficult to overcome due to the presence of phenyl rings number in the compound, the hydroxyl groups number in the aromatic cycle, and the bioavailability of polyphenols in food that depends on the pre- & post-harvest conditions and interactions with other compounds. These class compounds have bad absorption ability, slight solubility in water, and fast metabolism, so they need to be made into several types of pharmaceutical formulations that can increase bioavailability. Some polyphenols have low stability, so the choice of liposome form for polyphenol encapsulation is considered appropriate.

Hira Jamshaid 13/12/21 10.07
Deleted: al

Hira Jamshaid 13/12/21 10.07
Formatted: Highlight

Hira Jamshaid 13/12/21 10.07
Deleted: and

Hira Jamshaid 13/12/21 10.09
Deleted: activities as

Hira Jamshaid 13/12/21 10.10
Formatted: Highlight

Hira Jamshaid 13/12/21 10.11
Deleted: ,

However, it is also important to notice the characteristics of each polyphenol because polyphenols have various molecular structures where the ring number and hydroxyl number affect their solubility [7]. An example is a podophyllotoxin as an anti-mitosis that has high toxicity so that its use is limited [9]. To overcome this problem, the modification of the podophyllotoxin structure is carried out with the hope that its toxicity will be lower.

Resveratrol is contained in *Vitis vinifera*, labrusca, and muscadine as a polyphenol compound [10]. It has functioned as an anti-oxidant, anti-cancer, anti-inflammatory, and cardioprotective [11]. Resveratrol is slightly soluble in water with proper bioavailability, photosensitive [12], and fast metabolism [13]. Polymer nanoparticles, Zein-based nanoparticles, nanoemulsions, liposomes, cyclodextrins, and resveratrol multiple nanoencapsulation have been described to increase bioavailability and pharmacokinetic figures [14-19]. This polyphenol will improve solubility and chemical stability if it is formulated with dipalmytoyl-phosphatidylcholine or distearoyl-phosphatidylethanolamine-polyethylene glycol 2000. It also prolongs efficacy and improves protection from UV B when combined with P90G or dicetyl phosphate [7].

Curcumin (diferuloyl-methane) is practically slightly soluble in water and has low bioavailability, so it is made in the formulation of liposomes, phospholipid vesicles, and polymer-based nano formulations [20, 21]. Oral bioavailability is 9 times higher when curcumin is combined with piperine, which functions as an absorption enhancer [22]. In addition, curcumin colloid nanoparticles (theracurmin) have 27 times higher effectiveness and can inhibit alcohol poisoning [23]. Curcumin that is formulated in liposomes using soybean phosphatidylcholine, film hydration, and extruction (MLV) will prolong the antioxidant protective effect. On the other hand, when it is formulated using dimyristoyl phosphatidylglycerol and lyophilisate, then it will improve bioavailability and reduction of protease cancer incidence and have an antiangiogenic effect [7].

Quercetin, as a natural flavonoid in various vegetables and fruits, has 100 times more water solubility after being formulated as a polymer nanoparticle suspension dosage form [24]. Ampelopsin from *Ampelopsis grossedentata* has anti-oxidant, anti-inflammatory, anti-hypertensive, anti-microbial, hepatoprotective, anti-carcinogenic activities, and cough-relieving effects. This compound is slightly water-soluble and has very low permeability, so it is packaged in microemulsions to increase bioavailability, solubility, and penetration [25]. Quercetin is

Hira Jamshaid 13/12/21 10.12
Deleted: itself

Hira Jamshaid 13/12/21 10.13
Deleted: s

Hira Jamshaid 13/12/21 10.13
Deleted:

Hira Jamshaid 13/12/21 10.16
Deleted: contained

Hira Jamshaid 13/12/21 10.17
Formatted: Highlight

Hira Jamshaid 13/12/21 10.17
Deleted: activities as

formulated in liposomes using dipalmytoyl-phosphatidylcholine and lecithin that will increase solubility, bioavailability, and anti-tumor and antioxidant effect [7]. *Origanum dictamnus* extract has anti-oxidant and anti-microbial substances in consequence of large amounts of coumarin and flavones, in which they are formulated into liposomes to increase their activity [26].

Encapsulation which protects phytoconstituents can be used to reduce the instability of the active ingredient, to slow down its degradation, and to increase activity. For example, quercetin formulated in liposomes form with PEG in plasma has a life span of more than five hours [27], whereas quercetin formulated in polymer nanoparticles form has increased anti-oxidant activity, and quercetin encapsulated in eudragite nanoparticles (polymer nanoparticles) has high stability [28].

Some other polyphenols, such as catechin, fisetin, dehydro-silymarin, and silymarin increase bioavailability, solubility, chemical stability, and several activities in liposome form using epikuron/Tween, dioleoyl-phophatidylchooline/PEG 2000, soybean phosphatidylcholine, lecithin, and mannitol, respectively [7].

Application of a lipid bilayer in liposomes serves to increase the permeability of catechins. It occurs because of the geometric relationship between lipids in liposomes and insoluble encapsulation drugs (catechins) [7]. To date, no system generalizes the composition and encapsulation of lipids. Numerous researches have concentrated on the modification of liposome surface and its composition in enhancing the incorporation of insoluble drugs and enhancing well-defined target locations.

Terpenoid

Terpenoids are the most widespread group of compounds from natural substances and more than 40,000 have been identified. In general, the structure of terpenes is formed from isoprene units with its constituent groups in the form of cyclic unsaturated hydrocarbons in at variance degrees of oxygen. Terpenoids are grouped because of the number of isoprene units into monoterpenes (one isoprene), sesquiterpenes, diterpenes (two isoprene), sesquiterpenes, triterpenes (tri isoprene), and tetraterpenes (four isoprene). A variety of terpenoids have been found to have anti-cancer, anti-alzheimer [29], anti-microbial, anti-fungal, anti-parasitic, anti-allergic, anti-spasmodic, anti-hyperglycemic, anti-inflammatory, and have immunomodulatory properties [30].

Monoterpenes are the main classes of terpenoids that have 1 isoprene unit found in floral aromas, plants containing essential oils, and aromatic plants resins [31] which act as anti-tumor agents. Timokuinone is an active constituent of *Nigella sativa* as an anti-oxidant, anti-inflammatory, and anti-cancer [32,33]. However, the compounds have limitations that hinder pharmaceutical applications such as poor solubility, extreme lipophilicity, and instability to light and heat. Triterpenoids have more than 90 carbon skeletons with oxidative modification and skeleton glycosidation resulting in more diversities [34]. Ursolic acid (UA) and oleanolic acid (OA) are natural triterpenoids obtained by no less than 120 plants. OA has hepatoprotective, anti-inflammatory, anti-hyperlipidemic, anti-tumor, anti-viral whereas UA has anti-inflammatory, anti-hyperlipidemic, anti-hyperglycemic, hepatoprotective, anti-carcinogenic, neuroprotective, and anti-ulcer [35]. Their bioavailability is severely restricted by their slightly soluble in water.

Cucurbitacins are oxidized tetracyclic triterpenoids that are bitter and toxic. These compounds can be obtained in Rubiaceae, Cucurbitaceae, Desfontainiaceae, Scrophulariacea, Begoniaceae, Elaeocarpaceae, Polemoniaceae, Thymelaeaceae, Primulaceae, Brassicaceae, Sterculiaceae, Datiscaceae, and Rosaceae families. These compounds function as heterologous chemical secretions that maintain plants from outside biological disturbances [36] and are useful as anti-pyretic, anti-inflammatory, anti-tumor, anti-microbial, and analgesic [37].

Triptolide is an epoxide diterpenoid isolated from *Tripterygium wilfordii* and useful in polycystic kidney remedies, pancreatic carcinoma, autoimmune, rheumatism, leukemia, and psoriasis even though this compound has poor solubility and is toxic. Triptolide is prepared in a microemulsion system as poly [DL-lactic acid] [38] nanoparticles which are biocompatible and biodegradable for transdermal preparations. Triptolide has an irritating side effect on the gastric system, thus it is encapsulated in SLN so that the irritation can be minimized [39].

Cryptotanshinone is included in the quinoid diterpene class contained in the root of *Salvia miotiorrhiza* Bunge and is useful as anti-inflammatory, anti-bacterial, cytotoxic, anti-oxidative, anti-angiogenic and anti-parasitic, but has poor bioavailability due to water solubility. The bioavailability of cryptotanshinone administered orally will increase when prepared in solid nano lipid formulation [40].

Timoquinone is a monoterpene from *Nigella sativa* seeds that has anticancer activity [41], poor solubility, and high hydrophobicity. The preparation of an encapsulating thymoquinone formula with polymers [42], liposomes [43], and cyclo-dextrin [44] can solve this problem.

Alkaloid

The structural framework for alkaloids containing nitrogen atoms as part of the heterocyclic ring structure and have significant biological activity, for example, ephedrine for asthma, morphine for analgesics, and vinblastine for anticancer. Alkaloids vinblastine, vincristine, and vinorelbine cause microtubule disturbance effects and result in metaphase capture in dividing cells [45] so that a controlled release preparation can be formed which will proceed in a long-period exposure. However, these compounds have side effects that are toxic to hematology, causing wheezing, dyspnea, vomiting, nausea, constipation, fever, and chest pain or tumors. Investigators have recently reported that the preparation of liposome nanocarrier preparations on vinca alkaloids reduces these side effects [45,46].

Tetrandrine is a bis-benzylisoquinoline alkaloid that has anti-tumor activity and a non-selective calcium channel blocker. This compound has poor water solubility so its incorporation into the SLN system [47] can improve the formula. Paclitaxel in the gelatin nanoparticle formula is very effective for bladder cancer treatment because the release rate of the active ingredient and its solubility in aqueous media becomes easier [38]. This active ingredient has been recognized by the FDA and is marketed under the name Abraxane which is an effective and non-toxic cancer treatment.

Anabasine is a piperidine alkaloid isolated from the *Nicotiana glauca* tree which has high toxicity and its toxicity decreases after formulation with supramolecular nano-encapsulation [48]. Trigonelin is introduced into the chitosan nanoparticles through the formation of an ion complex between the trigonelin anionic carboxylic acid group and the chitosan cationic amine group to form particles less than 500 nm in size and inhibit tumor cell invasion [49].

Epiisopiloturine in *Jaborandi epiisopiloturine* leaves has activity towards adult, young, and egg of *Schistosoma mansoni* and is difficult to dissolve. Therefore, the structure of the liposomes is made to increase solubility by adding dipalmitoylphosphatidylcholine: cholesterol.

Antraquinone

Anthraquinone is a group of secondary metabolite compounds that can be obtained and available in abundance in natural materials. Anthraquinones are quinone derivatives of anthracents which have a basic structure of 9,10-anthraquinone dicetone. The presence of methoxyl, methyl, hydroxyl, and carboxyl groups attached to the core structure of 9,10-anthracenedione produces anthraquinone derivatives which have a wide spectrum of medicinal properties [50].

This group has the largest natural pigments of 700 compounds and 200 of them are isolated from plants (roots, rhizomes, fruits, and flowers), while the rest is from mosses and fungi [51]. It is widely used by humans as anti-tumor, anti-inflammatory, diuretic, antiarthritic, antifungal, antibacterial, antimalarial, antioxidant, and laxative [52].

Hypericin is a naphthodianthrone (anthraquinone) compound that is a natural photosensitizer, has high hydrophobicity, and has limited solubility. The formulation of hypericin solid lipid nanoparticle (Hy-SLN) and the hypericin polymeric nanoparticle suspension is evolved to acquire preferable photodynamic and photo detection [53].

Photodynamic therapy has many drawbacks such as poor water solubility and photosensitizer drug toxicity, thus anthraquinone derivatives derived from biotechnology and prepared classic nanocapsule formulations containing poly coating (PLGA) are capable of increasing photosensitizer cell uptake and are not toxic [54].

Radix rhei contains less efficient rhein, chrysophanol, physcione, emodin, and aloeemodin. Then, these compounds are formulated in the form of liposomes by the ethanol injection method so that the entrapment efficiency of the liposomal encapsulation is high [55].

NANOTECH FOR THE DELIVERY OF DIFFERENT PHYTOCONSTITUENTS

The problems faced in herbal formulations are slightly soluble in water, poor bioavailability, instability, and toxicity. The existence of nanotechnology is useful in overcoming some of the difficulties faced by the use of both synthetic and natural drug molecules. This technology has produced acceptable formulas such as embedded active phytochemicals. Various nanoparticle systems have been applied to support formulations such as encapsulation in the nanocarrier system and the deliverance of active compounds. The kinds of nanoparticles are dendrimers, solid lipid nanoparticles, liposomes, inorganic nanoparticles, microemulsions, polymer

nanoparticles, nanoflora, and others. This combination of technologies is competent to achieve the last stage of active compound examination thus enhancing the healthcare system.

Nano/submicro medicines in the size range from 1 to 1000 nm including liposomes, microspheres, solid lipid nanoparticles, nanoemulsions, and microemulsions (**Fig. 1**) are often used as herbal medicines topically and systemically [56]. This system has controlled hydrophobic and hydrophilic drug delivery, high drug-carrying capacity, better stability [56,57], higher superficies zone-to-volume proportion [57,58], and has a small size that supports high skin interactions, increases skin penetration, and extends the turnover term of molecules to the targeted sites through active targeting [57,59,60]. Many nanoparticle systems made of biodegradable biocompatible materials can be applied to encase toxic drugs and pass them to certain sites in the body.

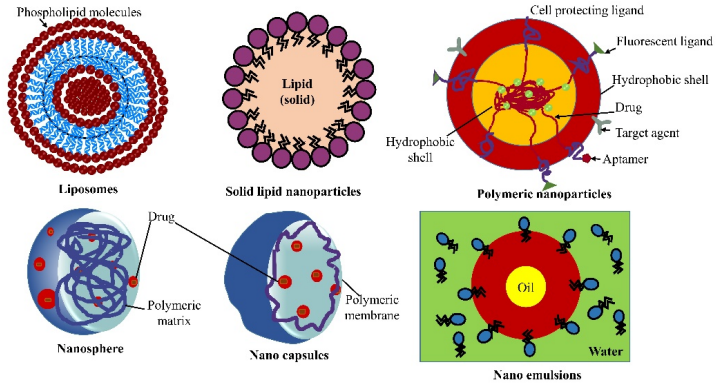

Figure 1. Overview of nano/sub microcarriers in herbal medicine [59].

Liposome

Liposomes are tiny vesicles consisting of one or more concentric lipid bilayers (phospholipids) and between which an aqueous medium is present. The name liposome comes from Greek, lipo, which means fat and soma, which means body, so liposomes are described as round objects which are mostly made of lipids. Liposomes are categorized as cationic, neutral, or anionic because of their type of surface charge. Variations in shape, size, and amount of lamellae contained in liposomes, are then classified as Unilamellar liposomes (ULs), small unilamellar

vesicles (SUV, 25–100 nm); multilamellar vesicles (MLV); large unilamellar vesicles (LUV, 100 nm to 1 m); multivesicle vesicles (MVV), and concheate vesicles (>1 m). Liposomes are easily produced by disrupting the lipid membrane in an aqueous medium through a sequence of extrusion (sonication) processes attended by a freezing-thaw process.

Liposomes have good biocompatibility and can improve physicochemical characteristics in pursuance of their lipid contexture and value. Vesicles are obtained from natural phospholipids that surround the water core. Liposomes are capable to trap both hydrophilic and lipophilic medications into the aqueous phase and lipidic bilayer so that the lipophilic drug will have high efficiency in the presence of the integrity of the membrane bilayer [33]. Plants and phytoconstituents that have been formulated using a liposome system can be seen in **table 1**.

Table 1. Liposome in several plants [4]

Plants	Carrier system	Methods	Effects
Cratylia mollis lectin	Soybean-phosphatidylcholine, cholesterol, & stearylamine	Positively charged surfaces	Degraded toxicity and escalated antitumor activity
Quercetin	Egg phosphatidylcholine & cholesterol	Negatively charged surfaces	Efficiency is between 60%–80%
Silymarin	Lecithin & cholesterol	Reverse evaporation	Improved bioavailability & absorption
Breviscapine	Phosphatidylcholine, cholesterol, phosphatidylglycerol & triolein/ tricaprylin	Double emulsification	Prolonged sustained delivery
Camptothecin	3,5-bis (dodecyloxy) benzoic (PO)-polyethylene glycol	Coating the surface	More efficient

A. arborescens essential oil	Hydrogenated and non-hydrogenated soy phosphatidylcholine	Positively charged MLVs and SUVs	A great ability to entice EO (60% - 74%)

Liposomes have an important role as a drug carrier system because they can encapsulate polar and non-polar compounds, have stability, have lengthy shelf life, are manageable, and their biocompatibility and degradability can be regulated. Some of the disadvantages of liposomes are their short half-lives and the integrity of the vesicles is not suitable for non-polar drugs. Phytosomes are phospholipids of nanoparticles that are covalently attached to phytochemicals [61].

Liposomes are flexible because they have a lipid structure that can be adjusted to drugs and a surface that can be converted for a specific target and time. The composition is adjusted to increase the drug solubility in the encapsulation system [7].

Microemulsion

Microemulsion (ME) is a fluid system consisting of a simple transparent emulsion with alcohol or medium chains (hexanol, pentanol) dissolved in an aqueous and comprising surfactants by the titration method. The presence of surfactants makes the system conditions thermodynamically stable with internal phase droplets at the nanoscale (10-100 nm). The active ingredients in the ME system will be distinct from the dispersion medium via the membrane or interface and transferred to an environment that can improve solubility, modular stability, or a bioavailability profile. Increased solubility and stability of ME are capable to deliver active constituents with different levels of lipophilis/hydrophilicity in the same formulation [62].

An example of the use of microemulsions is triptolide compound contained in the vines *Tripterygium wilfordii* Hook. F (Celastraceae). This plant has anti-inflammatory, anti-neoplastic, anti-fertility, and immunosuppressive effects, but its solubility in water is very poor and has a toxic effect. To improve it, it is formulated in isopropyl myristate TP as oil phase, aqueous as water phase, and Tween 80: 1,2-propylene glycol as surfactant: co-surfactant so that the permeation profile and anti-inflammatory test are increased [63]. In addition, the *Syagrus romanzoffiana* (Cham.) Glassman (Arecaceae) pulp extract is formulated in an o/w

nanoemulsion system with squalane as oil phase and a couple of ethoxylated surfactants with oleic alcohol as non-ionic surfactant which can increase its antioxidant activity.

Solid Lipid Nanoparticles and Nanostructured Lipid Carriers

Solid lipid nanoparticles (SLN) are colloid vehicle systems (50–1,000 nm) containing pure triglycerides and are combined with other colloid systems (emulsions, liposomes, and polymer nanoparticles) to eliminate shortages of active ingredients [64]. SLN has high physicochemical stability and protects from the degradation of labile drugs [65]. The resulting structures of this system are solid lipids or mixtures which are stabilized by surfactant [66].

The nanostructured lipid carrier (NLC) is a colloid system that comprises lipid and solid phases mixture to form an irregular liquid lipid matrix, increase the encapsulation efficiency, and minimize the active particles excretion during encapsulation [67]. The solid lipid phases put on the NLC system are glyceryl dilauric, stearic acid, hydrine, cetyl alcohol, and glyceryl monostearate while the liquid phases are caprylic/capric acid, oleic acid, and glyceryl monodicaprylic. Generally, the manufacture of NLC systems requires 5% of the active ingredient to the initial precursor mixture to produce a drug efficiency of about 3%-4% orally and 70% topically [68].

Table 2. Nanostructured Lipid Carriers and Solid Lipid Nanoparticles in several plants [4]

Constituents	SLN/NLC formulation	Methods	Effects
Quercetin	SLNs (glyceryl monostearate, & soy lecithin)	Emulsification-sonification	Controlled release, increases bioavailability to five times higher, and enhances absorption in the intestine
	SLNs (glyceryl dibehenate & oleic acid)	Microemulsification	Increases efficiency (92.33%) and stability and improves oral bioavailability
	NLCs (glyceryl	Emulsion	Promotes permeation,

	monostearate, stearic acid, & soy lecithin)	evaporation-sonification	increases the amount of substances that resisted in both epidermis and dermis, and enhances the anti-inflammatory and anti-oxidant activities
	NLCs	Probe ultrasonication	Excellent stability
Triptolide (*Tripterygium wilfordii*)	SLNs (tristearin glyceride & stearic acid)	Microemulsification	Improves solubility and absorption into skin.
Camptothecin	SLNs (cetyl palmitate & polysorbate 80)	Microemulsification	Increases bioavailability
Curcuminoid	SLNs (stearic acid & glyceryl monostearate)	Microemulsification	Improves the stability

The methods of SLN and NLC formulation are, such as high-pressure homogenization (HPH), emulsification-sonification, microemulsions, and solvent evaporation-emulsification techniques.

- HPH method is carried out by melting the lipids so that the medicine is homogeneously dispersed in the liquid lipid and added to the hot surfactant solution so that it is homogeneously dispersed (pre-emulsified) with the help of a sharp mixer. Then, the nanoemulsion is cooled at room temperature to form crystals. The cold HPH method is the same as hot HPH but the crystallization process uses liquid nitrogen and this technique is safe for hydrophilic or thermolabile drugs.
- The emulsification-sonification method is carried out by dissolving the active ingredient in a thawed solid lipid, adding a warm water surfactant solution, and then homogeneously dispersing it using a high shear mixer. The oil emulsion formed is separated using a sonicator probe according to nanoemulsion size and cooled.

- The microemulsion method dissolves the active ingredient in solid lipid and aqueous surfactant/cosurfactant solution that is added with light agitation to gain a clear microemulsion. Then, it is dissolved in cold water (2-10^{o}C) with light agitation and immediately crystallized to form SLN.
- The solvent-evaporation-emulsifying method works by how the lipids are dissolved in an organic solvent such as chloroform/cyclohexane and emulsified with aqueous surfactants under continuously stirring.

Utilization of Nanostructured Lipid Carriers and Solid Lipid Nanoparticles in few plants will be observed in **table 2**.

Inorganic Nanoparticles

Inorganic nanoparticles come from inorganic compounds such as ceramics, silver, carbon, and gold. These systems are classified into:

- Transition metal nanoparticles (Au, Ti, Pt)

  Transition metals do as medications in case there is excitation by a radiance which damages DNA and/or modifies proteins, increases lipid peroxidation, then destroys the microenvironment of the cell causing death. This method can be utilized for the treatment of cancer, carriers of site-specific toxic drugs [69], and potent catalysts.

- Ceramic nanoparticles (oxides, nitrides, and carbides with silica)

  The system can be used as a hollow or core-shell coated with a biodegradable and biocompatible polymer that enhances targeted delivery properties.

- Carbon nanoparticles.

Liquid crystalline systems

Liquid crystal (LC) is a phase distinct in the state between the crystalline solid and the isotropic liquid (mesophase) of the condensed structure. Mesophases that are cubic or hexagonal are classified into lyotropic liquid crystals (LLCs) and thermotropic liquid crystals (TLC) [70]. TLC is a mesophase molecule that depends on a specific temperature to convert it into an isotropic liquid. On the other hand, LLC is an amphiphilic molecule micelle that has a tiny polar (hydrophilic) and a big apolar oxtail (hydrophobic). Mesophase can be identified using low-

angle X-ray scattering (SAXS), low-angle neutron scattering (SANS), cryofracture electron microscopy, neutron diffraction, and reflected light microscopy [71].

LC application on herbal medicine is very advantageous because it is stable, easy to interact with certain targets optimally, a reliable, effective, and safe drug delivery system, distribution is evenly distributed with the selected route of administration, and has low side effects [72]. Vegetable oil is the most useful plant component for the development of this LC system because of its small molecular weight and poor viscosity. Vegetable oils produce low occlusion so they can easily penetrate the skin and increase the loading of therapeutic agents [73].

Santos and Rocha-Filho prove the effect of carbon bond length and the amount of ethylene oxide groups on the stability of the nonionic emulsion in vegetable oils and recommend the use of vegetable oils from apricot (*Prunus armeniaca*), pequi (*Caryocar brasiliense*), avocado (*Persea americana*), cupuassu (*Theobroma grandiflorum*), Brazil nuts (*Bertholletia excelsa*), mari-gold (*C. officinalis*), andiroba (*Carapa guyanensis*), passion fruit (*Passiflora edulis*), and Buriti (*Mauritia flexuosa*). For LC lamellar crystal stage, polyoxyethylene stearyl ether (Steareth-2; HLB: 4.7) and polyoxyethylene cetyl stearyl ether (Ceteareth-5; HLB: 9.2) are as surfactants and distilled water is as water phase. Liquid crystal systems can be used to overcome formulation limitations in plants and phytoconstituents (**Table 3**).

Table 3. Liquid crystalline systems in several plants [4]

Plants	Carrier system	Methods	Effects
Andiroba (*Carapa guyanensis* Aubl.)	• Oily phase: dicetyl phosphate, cetearyl alcohol, ceteth-10 phosphate • Aqueous phase: distilled water & PEG-12 Dimethicone	Silicone (surfactant)	Formulation viscosity, or rheological stability
Peach essential oil (*Prunus persica*)	LCs	Oil in water emulsions (o/w)	Improve physical stability

Annatto oil (*Bixa orellana*)	• Aqueous phase: Distilled water • Surfactant: oleth-20	Hydrophilic/lipophilic balance (HLB)	To construct LC
Marigold oil (*Calendula officinalis*)	• Aqueous phase: Distilled water • Surfactant: nonionic	HLB	Stable formulation
Marigold oil (*C. officinalis*)	• Aqueous phase: Distilled water • Surfactant:polyoxyethylene alkyl / stearyl ethers	Lamellar LC phases	Stability

Polymer Nanoparticles

Polymer nanoparticles are formulations made from polymers that are readily biodegradable and are biocompatible so that they are suitable as drug delivery systems because they are easy to control and target [74]. The colloid system of nanoparticles acts as a vector to manage the drug delivery, and targets it to a specific location. This system can escalate the constituents solubility, lower the therapeutic dose, and improve the absorption of the active components. This system can be applied to the blood because it is non-activate neutrophils, steady, non-immunogenic, non-toxic, non-thrombogenic, non-inflammatory, and avoids the reticuloendothelial route. Natural ingredients are preferably made in this system because of their capability to provide several active compounds with a similar carrier, intensify place time in the body, supply a continuous delivery system, and reduce side effects.

Polymer nanoparticles hold a diameter scale between 10–1,000 nm to facilitate the release of active substances on the target, increase bioavailability, and reduce side effects [75]. The shape of the nanoparticles is differentiated based on their composition and structural organization in the form of nanocapsules (NCs) and nanospheres (NSs). NCs has an oil core and is circled by a polymeric membrane so that the active constituents will be soaked up by the polymeric membrane and then dispersed in the oil base. NSs have a polymer structure so that the active

ingredients will be retained or absorbed. The types of polymers that are widely applied are copolymers with glycolic acid (PLGA) and poly-L-lactic acid (PLA) [76].

Table 4. Polymer Nanoparticles in several plants [4]

Plant/constituents	**Parts**	**Carrier system**	**Effects**
Phytolacca decandra	Root	PLGA-encapsulated forms (NPD)	Bioavailability is increased and preferable chemopreventive therapy toward lung cancer is generated
Ocimum sanctum	Leaves	Sodium alginate chitosan nanoparticles (OSN)	Better and more durable antimicrobial activity
Curcuma longa (curcumin)	Rhizome	poly(ethylene glycol) mono-acrylate, N-vinyl-2-pyrrolidone, and N-isopropylacrylamide	Has a great measure distribution of 50 nm and is easily dispersed in aqueous media.
		Encapsulated in PLGA nanospheres,	The encapsulation usefulness is 90.88%, the average particle size is 45 nm and is simply dissolved in an aqueous without surfactant
Magnolia officinalis (honokiol)	Bark, leaves	HN-loaded polymeric nanoparticles	Low hydrophobicity and free HN
Gelsemium sempervirens J. St.-Hil (coumarin)	Leaves	Polymeric nanocapsules	Better bioavailability than the free active constituent

Harungana madagascariensis Lam. Ex Poir	Leaves	Poly (D,L-lactide-co-glycolide) (PLG) nanoparticles	The bacterial growth is reduced
Cuscuta chinensis Lam.	Seed	Nanosuspension	The antioxidant activity is increased
Ginkgo biloba (quercetin)	Leaves	• Polyvinyl alcohol (PVA) • Eudragit® E (EE) of Nanoprecipitation	Better yield and the efficiency of encapsulation is bigger than 99%.
Camptotheca acuminata Decne (camptothecin)	Bark	Hydrophobically modified glycol chitosan (HGC)	The loading efficiency exceeds 80%
Polygala senega	Rhizome	Encapsulated by PLGA.	Bioavailability is increased

The polymer nanoparticle method is categorized as dispersed monomer method using alkyl cyanoacrylate, in situ polymerization method, and polymer deposition methods using poly lactic acid-co-glycolic/PLGA, acrylic/methacrylate esters, poly-caprolactone/PCL, poly lactic acid/PLA, and methacrylic acid copolymers (**Table 4**). The product obtained by using these three methods is the aqueous colloid suspension which has the disadvantage of experiencing precipitation and unstable physicochemical. This can be overcome by sublimation (freeze-drying) which causes the substance to become dehydrated and prevents particle aggregation [74]. Physicochemical characterizations such as morphological assessment, particle size, molecular weight alocation, zeta potential, pH establishment, drug dose in nanostructures, drug deliver kinetics, and stability in a long period should be carried out after nanoparticles are formulated.

Dendrimers

Dendrimers are branched macromolecules with a highly symmetrical/regular nano-size with a homogeneous and monodispersed structure. Dendrimers are also described as nano-sized globular molecules with unique 3D shapes (**Figure 2**) which have low dispersity and

multivalence with compositions that can be modified according to the desired purpose. The structure is divided into core, branched repetitive unit layers, and corona. This drug delivery system is preferred because of its flexibility, shape, functional group, size, and amount of generations. In addition, it is also very attractive [77].

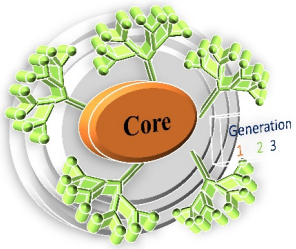

Figure 2. The 3D shapes of dendrimers [78]

The mechanism of dendrimer release in drug administration is (1) drug molecules are trapped in the dendrimer cavity so that the hydrophobic molecules' solubility increases, (2) drug molecules are conjugated with functional groups on the outer and their delivery rate is controlled. The system has advantages such as the ability to increase the diameter linearly and the ability to achieve a rounder shape [76]. In addition, dendrimers can prevent Aβ peptide fibrillation by blocking aggregation. This is evidenced by Wasiak et al. by modifying the aggregation of Aβ peptide and MAP-Tau protein in cationic phosphorus dendrimers [78]. Both peptides are the main conducive agents for DA. The presence of a desiccant in the dendrimers system may also reduce the toxicity of aggregated Aβ peptides. The formulation of nanoparticles of phytoconstituents can be seen in **table 5**.

Table 5. Nanoparticle formulation on phytoconstituents [79]

Phytoconstituents	**Nano/submicrocarriers**	**Remarkable effects**
Curcumin	SLNs	Oral bioavailability is more effective
Curcuminoids	SLNs	The release of the curcuminoids as anticancer and antioxidants is prolonged
Quercetin	Solid lipid nanoparticles	More and five times greater QU-SLN

	SLNs	bioavailability
	NLCs	NLCs have a goal ability, a prolonged-release, and a good potency for the dermal release system
	Liposomes	Antioxidant activity is increased and the drug release is 74 times higher
Glycyrrhizin acid	Nanoparticles	The bioavailability of anti-inflammatory and antihypertensive activity is improved
Taxel	Nanoparticles	Continuous blood circulation and huge accumulation in tumors
Camptothecin	Nanoparticles	Anticancer activity is improved
Berberine	Nanoparticles	Sustained drug release anticancer activity (Fukuda)
Silymarin	Liposome	More effective than silymarin suspension
Artemisinin	Nanocapsule	Anticancer activity

APPLICATION IN THERAPY

The nanoparticle drug formulations development has proven beneficial and provides opportunities to treat several diseases such as cancer, AIDS, HIV, nutraceutical delivery, and advances in diagnostic testing. The size of the nanoparticles varies from 100 to 500 nm. Nanoparticles can be improved to become intelligent systems, excellent packaging agents of therapeutic and imaging, and assuming stealth properties by manipulating the size, surface characteristics, and materials used. This system can pass drugs to the target tissues and give controlled release therapy according to a continuous target to reduce the amount of drug toxicity and improve patient obedience [80].

Cancer

Cancer is a complex disease to solve due to the ability of cells to divide and multiply rapidly and uncontrollably. Types of cancer therapy commonly used by patients, both through drugs and chemotherapy, cause side effects that destroy other normal cells like intestinal epithelium and hair follicles [81]. The nanoparticles development has offered a breakthrough in chemotherapy through goal medications delivery at the site of a tumor or a specific cells group to prevent toxic impact on another normal organ and tissues [82]. Micelles are the best way to dissolve an insoluble drug because the nucleus is hydrophobic and the shell is hydrophilic. The PEGylated micelle surface enhances the ability of the nanocarrier to pass through tumor blood vessels and inflamed tissue by passive transport, giving effect in a higher dose of tumor therapy. Examples of polymer micelles including anti-cancer medications are NC-6004, NK105, NK012, NK911, SP1049C [83], and Genexol-PM [84].

Nanoparticle therapy with the dendrimer system can increase the cytotoxic drugs therapeutic index by using biocomponents and lowering the face by PEGylation, glycosylation, acety-lation, and various amino acids [85,86]. Nanoparticles, namely Carbon nanotubes (CNTs), have allotropic forms of carbon with a cylindrical frame and a deepening of the number of the sheet in concentric cylinders, can be categorized as carbon nanotubes with associated walls (SWCNTs) and multiwalled carbonnanotubes (MWCNTs) [87,88]. Carbon nanotubes have a hollow interior that is highly hydrophobic so that medications insoluble water can easily pass.

Rhematoid

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease of the joints due to persistent polycarticular inflammation in the synovial tissue, which causes progressive deterioration of the articular cartilage and bone [89]. RA occurs due to genetic, and environmental factors [90], and an abnormal immune response leading to synovial inflammation and joint damage.

Currently available pharmaceutical drugs are administered via conventional dosage forms and provide therapeutic advantages only to a suboptimal level, thus posing challenges and barriers to the treatment of RA. This requires new drug delivery strategy design to the development of a useful, targeted and safe drug delivery system with better therapeutic performance [89,91]. Nanomedicines can perform the carriers of drug delivery for effective RA management because they have unique drug delivery characteristics and are considered a very promising alternative to

conventional drug therapy [92]. Among the several drug delivery routes available for RA, topical nanomedicines are more advantageous because of their greater skin retention ability, targeted specific actions, reduced drug doses, lower side effects increased acceptance, and higher patient adherence [91].

Oral administration of pomegranate extract is effective against cartilage damage because the extract contains ellagitannins, quercetin, ellagic acid, gallic acid, and polyphenols [93] by downregulatory activities against JNK-MAPK and NF-jB. Thymoquinone (TQ) from *Nigella sativa* seeds has shown beneficial effects on inflammatory disorders including IBD, RA, and osteoarthritis [94] through inhibition of serum IL-1b and TNF-a levels in RA. [95]. Resveratrol is a natural polyphenol compound obtained from grape skin (*Vitis vinifera*) and Polygonum cuspidatum root. Intra-articular resveratrol injection has shown potent action against arthritis by slowing IL-1-induced apoptosis, ROS, tumor protein (p53), LTB-4, PGE2, and MPPs in animal models [96]. Hesperidin is a citrus flavonoid reported to have therapeutic benefits from arthritis through inhibition of secondary leg swelling and downregulation of TNF-a production, IL-1, and IL-6 [97]. Then curcumin is a tetraterpenoid obtained from Curcuma longa which has anti-inflammatory, antioxidant, and anticancer activities [98]. Green Tea Extract (GTE) exerts antiarthritic effects due to the presence of nontoxic epigallocatechin-3 gallate (EGCG) through inhibition of IL-1-induced delivery of glycosaminoglycans and nitric oxide synthase stimulated by IL-1 (iNOS), nitric oxide, and JNK action [99]. Celastrol is a pentacyclic triterpene of *Trypterygium wilfordii* and has antitumour and anti-inflammatory effects through downregulation of caspase-1 and inhibition of NF-jb activation [100]. Gambogic acid (GA) is a polyprenylated xanthones containing resin derived from Garcinia hanburyi and Garcinia Morella as an antiarthritic molecule by inhibiting the secretion of IL-1b and TNF. Synomenine is an alkaloid obtained from *Sinomenium acutum*. It is effective for RA therapy by suppressing IL-6, MMP-2, and MMP-9 in an animal model of rheumatism [101]. Centella asiatica contains asiaticoside, madecassoside, centelloside, and asiatic acid (triterpenoids) which are active as anti-inflammatory [102].

The consolidation of phytoconstituents like resveratrol, gambogic acid, timokuinones, selastrol, hesperidin, curcumin, and polyphenols in a dose-dependent manner has great potential in RA pharmacotherapy through inflammatory mediators such as cytokines, NF-kb, nitric oxide (NO), chemokines, arachidonic acid (AA), adhesion molecules, and lipoxygenase (LOXs).

Phytoconstituents have several limitations such as non-uniform dosage and poor bioavailability, higher metabolism, and greater distribution characteristics. There are limited data available on the concentration of polyphenols in human tissue [103], namely 2-20%. The majority of polyphenols are metabolized directly by methylation, glucuronidation, sulfation, and elimination by the liver resulting in low bioavailability [103]. Oral administration of cumin causes poor plasma levels as appealed with intravenous administration [22]. Resveratrol is metabolized by the tiny intestine and its rapid metabolism [104] is detected in serum and plasma at a concentration of 491 90 ng/ml. Quercetin is detectable in plasma as glucuronides and sulfates unconjugated form [105]. Herbs for RA have limited solubility and permeability, which have a higher metabolism, do not have suitable dose, and have poor bioavailability [104,105]. This bioactive incorporation has low water solubility and high metabolism. These drawbacks can be overcome by using nano/submicrocarrier-based drug delivery technology, which maximizes increased bioavailability, greater stability, and better efficacy without systemic side effects [91].

To overcome curcumin's limitations, solid lipid nanoparticles are used effectively to lower leg volume through regulation of the oxide-inflammatory cascade and immunomodulators [106]. The development of proniosomes containing curcumin (curcumin incorporated into a nanoemulsion gel) by the transdermal route can increase skin permeation fourfold [107]. Poly (lactide-co-glycolide) (PLGA) polymer assisted nanoparticles on thymoquinone increase the entrapment efficiency to 97.5 [108]. Microemulsion based hydrogel on synomenine is able to suppress leg swelling through inhibition of TNF-a, IL-1, and PGE_2 [109]. Total paeony glucoside (TGP) incorporated into the microemulsion can increase poor oral bioavailability (3-4%) [110] to stability in GIT [111]. The development of nanosphere-based hydrogels and solid lipid nanoparticles on Tetrandrine has shown increased effectiveness [112]. In addition, the ethosome of this compound has a skin permeation 2.1 times higher than its liposome form [113]. *Tripterygium wilfordii* Hook F (TWHF) containing triptolide (TP) is incorporated into a microemulsion based hydrogel to increase its narrow therapeutic index [114]. The medical nano/submicron loaded in the phytoconstituent to reduce limitations in RA therapy is shown in **table 6**.

Table 6. Nano/submicron loaded to reduce limitations in RA therapy [91]

Phytoconstituents	Nano/submicrocarriers	Remarkable effects

Curcumin	Solid lipid nanoparticles	Greatly effective for arthritis treatments in rats by excellent decrease in paw volume via down-regulation of oxide-inflammatory and immune-modulatory cascade
	Nanoemulsion gel	Fourfold greater skin permeation and skin retention compared to curcumin solution in oil
	Proniosomes	Skin permeation through rat skin that is higher is found
Thymoquinone	Polymeric nanoparticles	The 97.5% entrapment efficiency (EE) is received. Furthermore, higher potency as compared to thymoquinone alone is obtained
Sinomenine	Microemulsion-based hydrogel	Higher beneficial effects are obtained which resulted by suppressing paw swelling via inhibition of TNF-a, IL-1, and PGE_2
Total glucosides of paeony (TGP)	Microemulsion	The bioavailability and stability problems are overcome by micro-emulsion, which also improves drug stability in GIT and enhances absorption
Tetrandrine	Nanospheres-based hydrogel	It enhances absorption
	Solid lipid nanoparticles	It enhances absorption
	Ethosomes	The 2.1 higher skin permeation is found as compared to liposomes

Triptolide (TP)	Microemulsion-based hydrogel	Good efficacy against RA is obtained. Furthermore, no significant toxicity is discovered throughout study.
	SLNs	Significant rat paw volume is reduced and a protective effect against hepatotoxicity is presented

Nutraceutical delivery

Nutraceuticals are standardized components derived from food and consumed as a complement to allopathic therapies and provide additional health benefits as well as reduce the risk of chronic disease [115]. The bioavailability and efficacy of nutraceuticals taken orally are influenced by the interaction of the matrix with food, their solubility in water, epithelial permeability, and degradation/metabolism[116]. They are lipophilic molecules that are soluble in fat (A, D, E, and K), and polyunsaturated lipids. Nanoparticle formulations in nutraceuticals [116,117] can reduce their limitations so that they can be used as anti-inflammatory, antioxidant, antiapoptotic, and antiangiogenic.

Table 7. Nutraceutical formulation [118]

Phytoconstituents	**Nano/submicrocarriers**	**Remarkable effects**
Hydrophobins (Hyd)- Vitamin D3	Nanoencapsulation	• Hyd is discovered to be a promising nano-transport of hydrophobic nutraceutical to food beverage enrichment • Hyd offers significant care for vitamin D3 toward the reduction
Folic acid with whey protein and commercial	Nanoencapsulation	Bigger encapsulation efficiency Increases folic acid stability Bioactive stabilization is increased

resistant starch		
DL-α-tocopheryl acetate and β-carotene	Pluronic-127 and poly-ε-caprolacotne envelop nanocapsule through emulsification-diffusion method (EDM)	EDM is a promising method to prepare nanoparticles for food materials
Vitamin D3 entrapped with whey protein NPs with different calcium concentration	Nanoencapsulation	Great Vitamin D3 stability can be applied in the clear beverage and not as an enriching agent
Calcium and folic acid	Duel nutraceutical nanomaterial	To supply a good content of important nutrient in human health
β-carotene, folic acid, curcumin and ergocalciferol	Protein-polysaccharide soluble nanocomplex	To increase the antioxidant activity
Carotenoids	Lipid nanocarriers	High potency for clinical applications of novel delivery system for lipophilic plant extracts
CoQ10	Lipid free nanoformulation	Effective transportation to increase the bioavailability of CoQ10 orally
Long chain fatty	Nanoemulsion	Nanoemulsion delivery systems increase

acids and CoQ10		the oral bioavailability of lipophilic nutraceuticals
Omega-3-fatty acids and oil-soluble vitamins	Biopolymeric nanogels	• Encapsulation and shield bioactive applied only for food-grade substance • The fabricated system remedies food and beverages quality
Curcumin	Organogel based nanoemulsion	Digestion of nanoemulsion is very speedy and perfect The oral bioavailability of curcumin improves Applied in dietary supplements, functional foods, and pharmaceutical industries
α-tocopherol	Supercritical assisted nanosuspension	Improves dissolution rate, bioavailability and stability
(-)-epigalocatechin-3-gallate	Protein-polyphenol coassemblies: Lactoferrin based NPs	• LF-EGCG-nanoparticles and submicrometer have purpose as EGCG protective transports to supervise other bioactive materials release. • LF-EGCG has potency to developing food formulation based on LF as a carrier of bioactive constituents
Eugenol and clove oil	COM and EM oil titration–precipitation	The formulation in microemulsion gives a delivery system for clove oil orally in homogenous, water-based and thermodynamically stable dose
Dextran and isoflavone	Enzymatic assisted inclusion complexation	• DMSO-water inclusion protocol is more suitable for delivering genistein

genistein	method	into enzymatically dextran • Increase the produce of nutraceuticals delivery by 11 to 141 folds due to the novel H-bonds establishment and the interaction of Vander walls

Nanotechnology applications for nutraceutical preparations are for nutrient delivery, food contact materials, nutrient bioavailability, security devices, sensor diagnostics, vitamin and mineral fortification and nanoencapsulation of flavor and aromas [118] while a summary of the potential formulations of nutraceuticals as nanomaterials can be seen in **table 7**.

Nanotechnology has a very important and powerful impact on modern life. The technological speed of using nanomedicine is carried out by utilizing several kinds of nanoparticles in the precaution, diagnosis, and many complex illness therapies. Herbal products that used to have many problems in the formulation and delivery of their active ingredients are now starting to see the advantages of nanotechnology application. Cosmetochem's Herbasec® has been launched as a liposomal standardized extract used in cosmetics for its antioxidant effect in preventing aging. Several other plants are also produced using nanomedicines such as white hibiscus, green tea, aloe vera, white tea, gourana, and liquorice root. There are also several phytochemicals produced for nanomedicines like triterpenes in *Centella asiatica*, visnadin in *Ammi visnaga*, silymarin and Silybin in milk thistle, vhamitenosides in Hawthorn blossoms, escin ß-sitosterol in horse chestnut, sericoside in *Terminalia sericea*, ginsenosides in *Panax ginseng*, polyphenols in grape seeds and green tea, ginkgo flavon glucosides, ginkgolides, and bilobalide in *Ginkgo biloba* [74]. This proves that nanotechnology for drug delivery is phytoconstituents future and opens an era to re-explore and investigate the full potency of traditional herbs. The advantages of using nanoscience about herbal medicine are:

- Increasing the solubility of active ingredients and bioavailability
- Lowering the side effects and toxicity of active ingredients
- Increasing the stability of active ingredients towards work targets
- Improving biocompatibility and reducing the toxicity of the formulations
- Increasing the safety of nanoparticles increases the therapeutic index of the drug

CONCLUSION

Poor absorption of some phytoconstituents because they are hydrophilic and unable to pass through cell lipid membranes can be overcome by applying nanoengineering such as phytosomes, liposomes, nanoemulsions, nanoparticles, solid lipid nanoparticles, and ethosomes in increasing solubility, bioavailability, pharmacological, stability, effectiveness, selectivity, and drug specificity of the bioactive constituents

ACKNOWLEDGEMENT: None

CONSENT OF PUBLICATION: None

CONFLICT OF INTEREST: None

REFERENCES

[1] Matijevic E. Fine particles in medicine and pharmacy. New York: Springer 2012.

[2] Vo TN, Kasper FK, Mikos AG. Strategies for controlled delivery of growth factors and cells for bone regeneration. Adv Drug Deliv Rev. 2012; 64(12): 1292–1309.

[3] Kohane DS. Microparticles and nanoparticles for drug delivery. Biotechnol Bioeng. 2007; 96(2):203–9.

[4] Bonifacio BV, Bento DP, Aparecido M, Ramos S, Negri K M, Bauab TM, et al. Nanotechnology-based drug delivery systems and herbal medicines: A review. Inter J Nanomedicine 2014; 9: 1–15.

[5] Bharali DJ, Siddiqui IA, Adhami VM, Chamcheu JC, Aldahmash AM, Mukhtar H, at al. Nanoparticle delivery of natural products in the prevention and treatment of cancers: Current status and future prospects. Cancers 2011; 3: 4024–45.

[6] Martens S, Mithöfer A. Flavones and flavone synthases. Phytochemistry 2005; 66: 2399–407.

[7] Mignet N, Seguin J, Chabot GG. Bioavailability of polyphenol liposomes: A challenge ahead. Pharmaceutics 2013; 5: 457–71.

[8] Mann J, Davidson RS, Hobbs JB, Banthorpe DV, Harborne JB. Natural products: Their chemistry and biological significance. Longman Group UK Limited, 1st edition 1994.

[9] Bruschi M, Orlandi O, Rindone M, Rindone B, Saliu F, Suarez-Bertoa R, et al. Podophyllotoxin and antitumor synthetic aryltetralines. Toward a biomimetic preparation. In: Mukherjee A. (ed.) Biomimetics learning from nature. InTech, 2010.

[10] Celotti E, Ferrarini R. Resveratrol content of some wines obtained from dried *Valpolicella grapes*: Recioto and amarone. J Chromatogr A 1996; 730(1–2): 47–52.

[11] Summerlin N, Soo E, Thakur S, Qu Z, Jambhrunkar S, Popat A. Resveratrol nanoformulations: Challenges and opportunities. Int J Pharm. 2015; 479(2): 282–90.

[12] Trela BC, Waterhouse AL. Resveratrol: Isomeric molar absorptivities and stability. J Agric Food Chem. 1996; 44: 1253–57.

[13] Walle T. Bioavailability of resveratrol. Ann NY Acad Sci. 2011; 1215: 9–15.

[14] Lindner GR, Santos DB, Colle D, Moreira ELG, Prediger RD, Farina M, et al. Improved neuroprotective effects of resveratrol-loaded polysorbate 80-coated poly(lactide) nanoparticles in MPTP- induced Parkinsonism. Nanomedicine 2015; 10(7): 1127–38.

[15] Penalva R, Esparza I, Larraneta E, González-Navarro CJ, Gamazo C, Irache JM. Zein-based nanoparticles improve the oral bioavailability of resveratrol and its anti-inflammatory effects in a mouse model of endotoxic shock. J Agric Food Chem. 2015; 63(23): 5603–11.

[16] Sessa M, Balestrieri ML, Ferrari G, Servillo L, Castaldo D, D'Onofrio N, et al. Bioavailability of encapsulated resveratrol into nanoemulsion-based delivery systems. Food Chem. 2013; 147: 42–50.

[17] Soo E, Thakur S, Qu Z, Jambhrunkar S, Parekh H, Popat A. Enhancing delivery and cytotoxicity of resveratrol through a dual nanoencapsulation approach. J Colloid Interface Sci. 2016; 462: 368–74.

[18] Venuti V, Cannava C, Cristiano MC, Fresta M, Majolino D, Paolino D, et al. A characterization study of resveratrol/sulfobutyl ether-b-cyclodextrin inclusion complex

and in vitro anticancer activity. Colloids Surf B Biointerf. 2014; 115: 22–8.

[19] Catania A, Barrajón-Catalán E, Nicolosi S, Cicirata F, Micol V. Immunoliposome encapsulation increases cytotoxic activity and selectivity of curcumin and resveratrol against HER2 overexpressing human breast cancer cells. Breast Cancer Res Treat. 2013; 1: 55–65.

[20] Mohanty C, Sahoo SK. The in vitro stability and in vivo pharmacokinetics of curcumin prepared as an aqueous nanoparticulate formulation. Biomaterials 2010; 31(25): 6597–611.

[21] Carvalho DM, Takeuchi KP, Geraldine RM, Moura CJ, Torres MCL. Production, solubility and antioxidant activity of curcumin nanosuspension. Food Sci. Technol. 2015; 35(1): 115–19.

[22] Shaikh J, Ankola DD, Beniwal V, Singh D, Kumar MNVR. Nanoparticle encapsulation improves oral bioavailability of curcumin by at least 9-fold when compared to curcumin administered with piperine as absorption enhancer. Eur J Pharm Sci. 2009; 37: 223–30.

[23] Sasaki H, Sunagawa Y, Takahashi K, Imaizumi A, Fukuda H, Hashimoto T, et al. Innovative preparation of curcumin for improved oral bioavailability. Biol Pharm Bull. 2011; 34(5): 660–65.

[24] Yen FL, Wu TH, Lin LT, Cham TM, Lin CC. Nanoparticles formulation of *Cuscuta chinensis* prevents acetaminophen-induced hepatotoxicity in rats. Food Chem Toxicol. 2008; 46: 1771–7.

[25] Solanki SS, Sarkar P, Dhanwani RK. Microemulsion drug delivery system: for bioavailability enhancement of ampelopsin. ISRN Pharmaceutics 2012;Article ID108164: 1–4.

[26] Gortzi O, Lalas S, Chinou I, Tsaknis J. Evaluation of the antimicrobial and antioxidant activities of *Origanum dictamnus* extracts before and after encapsulation in liposomes. Molecules 2007; 12: 932–45.

[27] Yuan Z, Chen L, Fan L, Tang M, Yang G, Yang H, et al. Liposomal quercetin efficiently suppresses growth of solid tumors in murine models. Clin Cancer Res. 2006; 12(10): 3193–9.

[28] Pool H, Quintanar D, Figueroa J, Figueroa, Bechara E, McClements D et al. Polymeric nanoparticles as oral delivery systems for encapsulation and release of polyphenolic compounds: Impact on quercetin antioxidant activity and bioaccessibility. Food Biophysics 2012; 7: 276–88.

[29] Gali-Muhtasib H, Diab-Assaf M, Boltze C, Al-Hmaira J, Hartig R, Roessner A et al. Thymoquinone extracted from black seed triggers apoptotic cell death in human colorectal cancer cells via a P53-Dependent mechanism. Int J Oncol. 2004; 25(4): 857–66.

[30] Thoppil RJ, Bishayee A. Terpenoids as potential chemopreventive and therapeutic agents in liver cancer. World J Hepatol. 2011; 3(9): 228–49.

[31] Rabi T, Bishayee A. Terpenoids and breast cancer chemoprevention. Breast Cancer Res and Treatment 2009; 115(2): 223–39.

[32] Kaseb AO, Chinnakannu K, Chen D, Sivanandam A, Tejwani S, Menon M, et al. Androgen receptor– and E2F-1–targeted thymoquinone therapy for hormone-refractory prostate cancer. Cancer Res. 2007; 67(16): 7782–8.

[33] Cheh lN, Chipitsyna G, Gong Q, Yeo CJ, Arafat HA. Anti-inflammatory effects of the *Nigella sativa* seed extract, Thymoquinone in pancreatic cancer cells. HPB (Oxford) 2009; 11(5): 373–81.

[34] Kushiro T, Shibuya M, Masuda K, Ebizuka Y. Mutational studies on triterpene synthases: Engineering lupeol synthase into *β*-Amyrin synthase. J Am Chem Soc. 2000; 122: 6816–24.

[35] Yang L, Sun Z, Zu Y, Zhao C, Sun X, Zhang Z et al. Physicochemical properties and oral bioavailability of ursolic acid nanoparticles using Supercritical Anti- solvent (SAS) Process. Food Chemistry 2012; 132: 319–25.

[36] Alghasham AA. Cucurbitacins–A promising target for cancer therapy. International Journal of Health Sciences 2013; 7(1).

[37] Lee DH, Iwanski GB, Thoennissen NH. Cucurbitacin: Ancient compound shedding new light on cancer treatment. The Scientific World Journal 2010; 10: 413–8.

[38] Zhang C, Gu C, Peng F, Liu W, Wan J, Xu H, et al. Preparation and optimization of Triptolide-loaded solid lipid nanoparticles for oral delivery with reduced gastric irritation. Molecules 2013; 18: 13340–56.

[39] Zhang N, Wardwell PR, Bader RA. Polysaccharide-based micelles for drug delivery. Pharmaceutics 2013; 5: 329–52.

[40] Hu LD, Xing Q, Meng J, Shang C. Preparation and enhanced bioavailability of Cryptotanshinone-loaded solid lipid nanoparticles. AAPS Pharm Sci Tech. 2010; 11(2): 582–87.

[41] Zihlif MA, Mahmoud IS, Ghanim MT, Zreikat MS, Alrabadi N, Imraish A, et al. Thymoquinone efficiently inhibits the survival of EBV-Infected B cells and alters EBV Gene expression. Integr Cancer Ther. 2013; 12(3): 257–63.

[42] Ravindran J, Nair HB, Sung B, Prasad S, Tekmal RR, Aggarwal BB. Thymoquinone poly(lactide-co-glycolide) nanoparticles exhibit enhanced antiproliferative, anti-inflammatory, and chemosensitization potential. Biochem Pharmacol. 2010; 79: 1640–7.

[43] Odeh F, Ismail SI, Abu-Dahab R, Mahmoud IS, Al Bawab A. Thymoquinonei liposomes: A study of loading efficiency and biological activity towards breast cancer. Drug Delivery 2012; 19(18): 371–7.

[44] Abu Dahab R, Odeh F, Ismail SI, Azzam H, Al Bawab A. Preparation, characterization and antiproliferative activity of Thymoquinon-β-cyclodextrin self assembly nanoparticles. Die Pharmazie 2013; 68: 939–44.

[45] Noble CO, Guo Z, Hayes ME, Marks JD, Park JW, Benz CC, et al. Characterization of highly stable liposomal and immunoliposomal formulations of vincristine and vinblastine. Cancer Chemother Pharmacol. 2009; 64: 741–51.

[46] Zhigaltsev IV, Maurer TN, Akhong Q, Leone R, Leng E, Wang J, et al. Liposome-encapsulated vincristine, vinblastine and vinorelbine: A comparative study of drug loading and retention. Int. J. Mol. Sci. 2012; 13: 12598–607.

[47] Li Y, Dong L, Jia A, Chang X, Xue H. Preparation and characterization of solid lipid nanoparticles loaded traditional chinese medicine. Int J Biol Macromolecules 2006; 38: 296–9.

[48] Gao Y, Yang X, Wang Y, Zhong Z, Hu Y, Wang Y. Supramolecular nano-encapsulation of anabasine reduced its developmental toxicity in Zebrafish. Frontiers in chemistry 2020; 8: 1–7.

[49] Jeong Y, Kim DH, Chung KD, Kim YH. Antitumor activity of Trigonelline-Incorporated chitosan nanoparticles. Journal of Nanoscience and Nanotechnology 2014; 14: 5633–7.

[50] Tutin F, Clewer HWB. The constituents of rhubarb. J Chem Soc Trans. 1911; 36: 946–67.

[51] Seigler DS. Plant secondary metabolism. Springer Science & Business Media, 2012.

[52] Chien S, Wu Y, Chen Z, Yang W. Naturally occurring anthraquinones: Chemistry and therapeutic potential in autoimmune diabetes. Evid Based Complement Alternat Med. 2015; 1–13.

[53] Limaa A, Pizzolb C, Monteirob F, Creczynski-Pasab T, Andradec G, Ribeiroc A, et al. Hypericin encapsulated in solid lipid nanoparticles: Phototoxicity and photodynamic efficiency. J of Photochemistry and Photobiology B: Biology 2013; 125(l): 146–54.

[54] Amantino CF, Baptista-Neto A, Badino AC, Antonio MP, Fernando CT, Primo L. Anthraquinone encapsulation into polymeric nanocapsules as a new drug from biotechnological origin designed for photodynamic therapy. Photodiagnosis and Photodynamic Therapy 2020; 31: 101815.

[55] Suo X, Liu Y, Wu Y, Li Y. Liposomal encapsulation of free anthraquinones in rhizoma et radix rhei and its quality control. Zhong Yao Cai 2010; 33(4): 614–6.

[56] Aboalnaja KO, Yaghmoor S, Kumosani TA, McClements DJ. Utilization of nanoemulsions to enhance bioactivity of pharmaceuticals, supplements, and nutraceuticals: nanoemulsion delivery systems and nanoemulsion excipient systems. Expert Opin Drug Deliv 2016; 21: 1–10.

[57] Song F, Tang J, Geng R, Hu H, Zhu C, Cui W, et al. Comparison of the efficacy of bone marrow mononuclear cells and bone mesenchymal stem cells in the treatment of osteoarthritis in a sheep model. Int J Clin Exp Pathol 2014; 7: 1415–26.

[58] Colmenares D, Sun Q, Shen P, Yue Y, McClements J, Park Y. Delivery of dietary

triglycerides to *Caenorhabditis elegans* using lipid nanoparticles: nanoemulsion-based delivery systems. Food Chem 2016; 202: 451–7.

[59] Rahman M, Kumar V, Beg S, Sharma G, Katare OP, Anwar F. Emergence of liposome as targeted magic bullet for inflammatory disorders: current state of the art. Artif Cells Nanomed Biotechnol 2016; 13: 1–12.

[60] Solans C, Izquierdo P, Nolla J, Azemar N, Celma MJG. Nano-emulsions. Curr Opin Colloid Interface Sci 2005; 10: 102–10.

[61] Kareparamban J, Nikam P, Jadhav A, Kadam V. Phytosome: A novel revolution in herbal drugs. Int J Research Pharm Chem. 2012; 2(2): 299–310.

[62] Sintov AC, Shapiro L. New microemulsion vehicle facilitates percutaneous penetration in vitro and cutaneous drug bioavailability in vivo. J Control Release 2004; 95(2): 173–83.

[63] Mei Z, Huabing C, Weng T, Yang Y, Yang X. Solid lipid nanoparticle and microemulsion for topical delivery of triptolide. Eur J Pharm Biopharm. 2003; 56(2): 189–96.

[64] Martins S, Costa-Lima S, Carneiro T, Cordeiro-da-Silva A, Souto EB, Ferreira DC. Solid lipid nanoparticles as intracellular drug transporters: an investigation of the uptake mechanism and pathway. Int J Pharm. 2012; 430(1–2): 216–27.

[65] Pardeike J, Hommoss A, Müller RH. Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. Int J Pharm. 2009; 366(1–2): 170–84.

[66] Naahidi S, Jafari M, Edalat F, Raymond K, Khademhosseini A, Chen P. Biocompatibility of engineered nanoparticles for drug delivery. J Control Release 2013; 166(2): 182–94.

[67] Wissing SA, Kayserb O, Müller RH. Solid lipid nanoparticles for parenteral drug delivery. Adv Drug Deliv Rev. 2004; 56(9): 1257–72.

[68] Puri A, Loomis K, Smith B, Lee J, Yoviovich A, Heidman E, et al. Lipid-based nanoparticles as pharmaceutical drug carriers: from concepts to clinic. Crit Rev Ther Drug Carrier Syst. 2009; 26(6): 523–80.

[69] Bhattacharyya S, Kudgus R, Bhattacharya R, Mukherjee P. Inorganic nanoparticles in cancer therapy. Pharm Res. 2011; 28(2): 237–59.

[70] Rossetti FC, Fantini MCA, Carollo ARH, Tedesco AC, Bentley MVLB. Analysis of liquid crystalline nanoparticles by small angle X-ray diffraction: evaluation of drug and pharmaceutical additives influence on the internal structure. J Pharm Sci. 2011; 100(7): 2849–857.

[71] Farkas E, Zelko R, Torok G, Racz I, Marton S. Influence of chlorhexidine species on the liquid crystalline structure of vehicle. Int J Pharm. 2001; 213(1–2): 1–5.

[72] Praça FSG, Medina WSG, Petrilli R, Bentley MVLB. Liquid crystal nanodispersions enable the cutaneous delivery of photosensitizer for topical PDT: fluorescence microscopy study of skin penetration. Curr Nanosci. 2012; 8(4): 535–40.

[73] Bernardi DS, Pereira TA, Maciel NR, Bortolo J, Viera GS, Oliveira GC, et al. Formation and stability of oil-in-water nanoemulsions containing rice bran oil: in vitro and in vivo assessments. J Nanobiotechnology. 2011; 9(44): 1–9.

[74] Khuda-Bukhsh AR, Bhattacharyya SS, Paul S, Boujedaini N. Polymeric nanoparticle encapsulation of a naturally occurring plant scopoletin and its effects on human melanoma cell A375. Zhong Xi Yi Jie He Xue Bao. 2010; 8(9): 853–62.

[75] Alexis F, Pridgen E, Molnar LK, Farokhzad OC. Factors affecting the clearance and biodistribution of polymeric nanoparticles. Mol Pharm. 2008; 5(4): 505–15.

[76] Senthil KP. Nano-drug delivery system: applications in veterinary medicine and animal health. Int J Sci Environ Technol. 2016; 5: 4447–51.

[77] Çetin M, Aytekin E, Yavuz B, Bozdag˘-Pehlivan S. Nanoscience in targeted brain drug delivery. In importance and application of nanotechnology-based brain drug delivery systems. Drug Delivery across the Blood-Brain Barrier 2017; 117–147.

[78] Wasiak T, Ionov M, Nieznanski K, Nieznanska H, Klementieva O, Granell M, et al. Phospho- rus dendrimers affect Alzheimer's (Aβ1-28) peptide and MAP-Tau protein aggregation. Mol Pharm. 2012; 9(3): 458–69.

[79] Bhavsar S. Application of nanotechnology for phytoconstituents: Review. Arch Nano 2018; 1(1): 6–7.

[80] Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology.

Saudi Pharmaceutical Journal 2018; 26: 64–70.

[81] Baudino TA. Targeted cancer therapy: the next generation of cancer treatment. Curr Drug Discov Technol. 2015; 12(1): 3–20.

[82] Shen B, Ma Y, Yu S, Ji C. Smart multifunctional magnetic nanoparticle-based drug delivery system for cancer thermo-chemotherapy and intracellular imaging. ACS Appl. Mater Interf. 2016; 8(37): 24502–8 .

[83] Oerlemans C, Bult W, Bos M, Storm G, Nijsen JFW, Hennink WE. Polymeric micelles in anticancer therapy: targeting, imaging and triggered release. Pharm. Res. 2010; 27: 2569–89.

[84] Zhang X, Huang Y, Li S. Nanomicellar carriers for targeted delivery of anticancer agents. Ther Deliv 2014; 5(1): 53–68.

[85] Baker JR. Dendrimer-based nanoparticles for cancer therapy. Hematol Am Soc Hematol Educ Program 2009; 708–19.

[86] Cheng Y, Zhao L, Li Y, Xu T. Design of biocompatible dendrimers for cancer diagnosis and therapy: current status and future perspectives. Chem Soc Rev 2011; 40(5): 2673–703.

[87] Rastogi V, Yadav P, Bhattacharya SS, Mushra AK, Verma N, Verma A, et al. Carbon nanotubes: an emerging drug carrier for targeting cancer cells. J Drug Deliv. 2014; 670815.

[88] Sanginario A, Miccoli B, Demarchi D. Carbon nanotubes as an effective opportunity for cancer diagnosis and treatment. Biosensors 2017; 7(1): 9.

[89] Anderson KO Bradley LA, Young LD, McDaniel LK, Wise CM. Rheumatoid arthritis: review of psychological factors related to etiology, effects, and treat- ment. Psychol Bull 1985; 98: 358–87.

[90] Scrivo R, Franco MD, Spadaro A, Valesini G. The immunology of rheumatoid arthritis. Ann N Y Acad Sci. 2007; 1108: 312–22.

[91] Rahman M, Beg S, Verma A, Abbasi FA, Anwar F, Saini S, et al. Phytoconstituents as pharmacotherapeutics in rheumatoid arthritis: challenges and scope of

nano/submicromedicine in its effective delivery. Journal of Pharmacy and Pharmacology 2017; 69: 1–14.

[92] Albuquerque J, Moura CC, Sarmento B, Resi S. Solid lipid nanoparticles: a potential multifunctional approach towards rheumatoid arthritis theranostics. Molecules 2015; 20: 11103–18.

[93] Rasheed Z, Akhter NHT. Pomegranate extract inhibits the interleukins-1b- induced activation of MKK-3, p38 a-MAPK and transcription factor RUNX-2 in human osteoarthritis chondrocytes. Arthritis Res Ther 2010; 12: R195.

[94] Umar S, Hedaya O, Singh AK, Ahmed S. Thymoquinone inhibits TNF-alpha-induced inflammation and cell adhesion in rheumatoid arthritis synovial fibroblasts by ASK1 regulation. Toxicol Appl Pharmacol 2015; 287: 299–305.

[95] Ahmed A, Husain A, Mujeeb M, Khan SA, Najma AK, Siddique NA, et al. A review on therapeutic potential of *Nigella sativa*: a miracle herb. Asian Pac J Trop Biomed 2013; 3: 337–52.

[96] Baur JA, Sinclair DA. Therapeutic potential of resveratrol: the in vivo evidence. Nat Rev Drug Discov 2006; 5: 493–506.

[97] Umar S, Kumar A, Sajad M, Zargan J, Ansari M, Ahmad, et al. Hespiridin inhibits collagen induced arthritis possibly through suppression of free radical load and reduction in neutrophil activation and infiltration. Rheumatol Int 2013; 33: 657–63.

[98] Funk JL, Oyarzo JN, Frye JB, Chen G, Lantz RC, Jolad SD, et al. Turmeric extracts containing curcuminoids prevent experimental rheumatoid arthritis. J Nat Prod 2006; 69: 351–55.

[99] Ahmed S. Green tea polyphenol epigallocatechin 3-gallate in arthritis: progress and promise. Arthritis Res Ther 2010; 12: 208.

[100] Salminen A, Lehtonen M, Paimela T, Kaarniranta K. Celastrol: molecular targets of thunder god vine. Biochem Biophys Res Commun 2010; 394: 439–42.

[101] Tong B, Yu J, Wang T, Dou Y, Wu X, Kong L, et al. Sinomenine suppresses collagen-induced arthritis by reciprocal modulation of regulatory T cells and Th17 cells in gut-

associated lymphoid tissues. Mol Immunol 2015; 65: 94–103.

[102] Wang T, Wei Z, Dou Y, Yang Y, Leng D, Kong L, et al. Intestinal interleukin-10 mobilization as a contributor to the anti-arthritis effect of orally administered madecassoside: a unique action mode of saponin compounds with poor bioavailability. Biochem Pharmacol 2015; 94: 30–8.

[103] Siddiqui MZ. Boswellia serrata, a potential anti-inflammatory agent: an overview. Indian J Pharm Sci 2011; 73: 255–61.

[104] Wenzel E, Somoza V. Metabolism and bioavailability of trans-resveratrol. Mol Nutr Food Res 2005; 49: 472–81.

[105] Morand C, Crespy V, Manach C, Besson C, Demigné C, Rémésy C. Plasma metabolites of quercetin and their antioxidant properties. Am J Physiol 1998; 275: R212–9.

[106] Arora R, Kuhad A, Kaur P, Chopra. Curcumin loaded solid lipid nanoparticles ameliorates adjuvant induced arthritis in rats. Eur J Pain 2015; 19: 940–52.

[107] Kumar K, Rai AK. Proniosomal formulation of curcumin having anti- inflammatory and anti-arthritic activity in different experimental animal models. Pharmazie 2012; 67: 852–7.

[108] Singh A, Ahmad I, Akhter S, Ahmad MZ, Igbal Z, Ahmad J. Thymoquinone: major molecular targets, prominent pharmacological actions and drug delivery Concerns. Curr Bioact Comp 2012; 8: 334–44.

[109] Zhang X, Zhu H, Meng S, Pan X. Preparation of sinomenine microemulsion and its transdermal absorption. Zhongguo Zhong Yao Za Zhi 2007; 32: 2007–10.

[110] Zheng YQ, Wei W. Total glucosides of paeony suppresses adjuvant arthritis in rats and intervenes cytokines signaling between different types of synoviocytes. Int Immunopharmacol 2005; 5: 156 –73.

[111] Wang X, Xue M, Gu J, Fang X, Sha X. Transdermal microemulsion drug delivery system for impairing male reproductive toxicity and enhancing efficacy of *Tripterygium Wilfordii* Hook f. Fitoterapia 2012; 83: 690–8.

[112] Li S, Ji Z, Zou M, Nie X, Shi Y, Cheng G. Preparations, characterization,

pharmacokinetics and tissue distribution of solid lipid nanoparticles loaded with tetrandrine. AAPS Pharm Sci Tech 2011; 12: 1011.

[113] Fan C, Li X, Zhou Y, Zhao Y, Ma S, Li W. Enhanced topical delivery of tetrandrine by ethosomes for treatment of arthritis. Biomed Res Int 2013; 2013: 161943.

[114] Chen H, Chang X, Weng T, Zhao X, Gao Z, Yang Y, et al. A study of microemulsion systems for transdermal delivery of triptolide. J Controlled Release 2004; 98: 427–436.

[115] Aggarwal BB, Van Kuiken MEV, Iyer LH, Harikumar KB, Sung B. Molecular targets of nutraceuticals derived from dietary spices: potential role in suppression of inflammation and tumorigenesis. Exp. Biol. Med. (Maywood) 2009; 234(8): 825–49.

[116] McClements DJ, Li F, Xiao H. The nutraceutical bioavailability classification scheme: classifying nutraceuticals according to factors limiting their oral bioavailability. Ann Rev Food Sci Technol. 2015; 6: 299–327.

[117] Acosta E. Bioavailability of nanoparticles in nutrient and nutraceutical delivery. Curr Opin Colloid Interface Sci. 2009; 14(1): 3–15.

[118] Gopi S, Amalraj A, Haponiuk JT, Thomas S. Introduction of nanotechnology in herbal drugs and nutraceutical: A Review J Nanomedine Biotherapeutic Discov. 2016; 6(2): 1–8.

rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Book: COVERING LETTER 1ST Galley Proofs | BMS-APHNT-2021-HT1-2938-1

2 messages

Ram Sahu <ramsahu79@gmail.com> Mon, Feb 21, 2022 at 7:41 PM
To: Doaa Al-Ahora <dalahora@ksu.edu.sa>, Ayodeji Ajayi <aajayi22@lautech.edu.ng>, "Dr. Sudarshan Singh" <sudarshansinghi10@gmail.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, "Dr.Ruby John Anto" <rjanto@rgcb.res.in>, sharmadibru@gmail.com, Sunita M <sunita3481@gmail.com>, prashardeepak99@yahoo.in, subhashis.ooty@gmail.com, "Dr. Anupom Borah" <anupomborah@gmail.com>, harsha1975@gmail.com, vishal trivedi <vishaltrivediqa@gmail.com>, "SH. VINOD NAUTIYAL" <vnautiyal@gkv.ac.in>, "Dr.Mahadeva Rao" <raousm@gmail.com>, raousm@unisza.edu.my, dr_santosh@msu.edu.my, ERWIN FALLER <erwinfaller1007@gmail.com>, "Erwin M. Faller" <emfaller@ceu.edu.ph>, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, "jiyauddin_khan@msu.edu.my" <jiyauddin_khan@msu.edu.my>, uditaagrawal.phama@gmail.com, Andang MIATMOKO <andang-m@ff.unair.ac.id>, pharm.anas.alhamdany@uomustansiriyah.edu.iq, SRIJA SUR <sursrija0714@gmail.com>, vivek dave <attachvivek@gmail.com>, priya shrivastava <shrivastavap007@gmail.com>

Dear Authors
Greetings
We are pleased to inform you all that our book has been accepted and received a gallery proof from the publisher. We have attached the gallery proof of the book for your information.
Please check your chapter for typesetting, editing, completeness, and correctness of text, tables, and figures. If your chapter needs to be corrected, please send us the list of corrections in the following format (doc. file) as an attachment to your e-mail by tomorrow.

Listed below is the editor's message:

The composed version of your manuscript is attached. I shall be grateful if you could kindly carefully check the composed version for any potential errors, missing lines/paragraphs and errors in figures/diagrams etc.

The uploaded proofs have been prepared directly from the final manuscript provided by you. However, in the transformation process, certain errors may have occurred due to a difference in the softwares used for which the Composing Department is not liable. The PDF version may distort your original figures. Therefore kindly check them carefully. All figures will be reproduced directly from your supplied soft copies. The resolution of the figures will be exactly the same as supplied to us with the original manuscript (except chemical structures). All references must be complete and accurate.

Moreover, as a part of the publication process, the manuscript has undergone copyediting for generally minor grammatical inconsistencies and specifically for some significant ambiguities (where necessary), to bring in clarity to the content. You are therefore requested to read the proofs thoroughly and send approval for all the corrections made in order to ensure that the original meaning of the content has not been altered in case of significant changes in the text.

Kindly return the corrected proofs of the manuscript within 24 hours. On receipt of your reply, the manuscript will be finalized for printing.

Regards,

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA

09893577279

2 attachments

Rebuttal.docx
14K

Gallery Proof of Book.pdf
8578K

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Wed, Feb 23, 2022 at 7:21 AM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr. Ram,

Thank you for helping to receive this book chapter.
I hereby send some writing errors and also pictures in chapter 4.

Best Regards,

Retno Widyowati, PhD
[Quoted text hidden]

Rebuttal Ch. 4.docx
992K

rr retno widyowati <rr-retno-w@ff.unair.ac.id>

Revised Galley Proofs of book | BMS-APHNT-2021-HT1-2938-1

3 messages

Ram Sahu <ramsahu79@gmail.com> Tue, Mar 8, 2022 at 6:21 PM
To: Doaa Al-Ahora <dalahora@ksu.edu.sa>, Ayodeji Ajayi <aajayi22@lautech.edu.ng>, "Dr. Sudarshan Singh" <sudarshansinghi10@gmail.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, "Dr.Ruby John Anto" <rjanto@rgcb.res.in>, sharmadibru@gmail.com, Sunita M <sunita3481@gmail.com>, prashardeepak99@yahoo.in, subhashis.ooty@gmail.com, "Dr. Anupom Borah" <anupomborah@gmail.com>, "N. Sree Harsha" <harsha1975@gmail.com>, vishal trivedi <vishaltrivediqa@gmail.com>, "SH. VINOD NAUTIYAL" <vnautiyal@gkv.ac.in>, "Dr.Mahadeva Rao" <raousm@gmail.com>, raousm@unisza.edu.my, dr_santosh@msu.edu.my, ERWIN FALLER <erwinfaller1007@gmail.com>, "Erwin M. Faller" <emfaller@ceu.edu.ph>, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, "jiyauddin_khan@msu.edu.my" <jiyauddin_khan@msu.edu.my>, uditaagrawal.phama@gmail.com, Andang MIATMOKO <andang-m@ff.unair.ac.id>, pharm.anas.alhamdany@uomustansiriyah.edu.iq, SRIJA SUR <sursrija0714@gmail.com>, vivek dave <attachvivek@gmail.com>, priya shrivastava <shrivastavap007@gmail.com>, abbma71@gmail.com, ABU MD ASHIF IKBAL <abumd97@gmail.com>

Dear Authors
Greetings
The publisher has revised the gallery proof and divided the book into two volumes. The gallery proof of both volumes and rebuttal attached for your reference.
Please check your chapter for typesetting, editing, completeness and correctness of text, tables and figures **(must not be blurred)**. Also check the **content section (correct citation of your chapter and its content)** and the **list of contributors section (are the details of your team members mentioned or not)**.

If your chapter needs to be corrected, please send us the list of corrections in the following format (doc. file) as an attachment to your e-mail by tomorrow.

Regards,

--
Dr. RAM SAHU
Assistant Professor,
Department of Pharmaceutical Sciences,
Assam University (A Central University),
Silchar-788011 (AS), INDIA
09893577279

3 attachments

Rebuttal.docx
14K

Volume 2 Book Gallery proof.pdf
3172K

Volume 1 Book Gallery proof.pdf
3536K

rr retno widyowati <rr-retno-w@ff.unair.ac.id> Wed, Mar 9, 2022 at 4:35 AM
To: Ram Sahu <ramsahu79@gmail.com>

Dear Dr. Ram,

My chapter is ok and thank you very much

Best regards,

Retno Widyowati, PhD

Dikirim dari iPhone saya

> Pada 8 Mar 2022, pukul 18.21, Ram Sahu <ramsahu79@gmail.com> menulis:
>
> [Quoted text hidden]
> <Rebuttal.docx>
> <Volume 2 Book Gallery proof.pdf>
> <Volume 1 Book Gallery proof.pdf>

DR ERWIN FALLER <erwinfaller1007@gmail.com> Mon, Mar 14, 2022 at 8:37 AM
To: Ram Sahu <ramsahu79@gmail.com>
Cc: Doaa Al-Ahora <dalahora@ksu.edu.sa>, Ayodeji Ajayi <aajayi22@lautech.edu.ng>, "Dr. Sudarshan Singh" <sudarshansinghi10@gmail.com>, rr retno widyowati <rr-retno-w@ff.unair.ac.id>, Nurul Asma Abdullah <nurulasma@usm.my>, "Dr.Ruby John Anto" <rjanto@rgcb.res.in>, sharmadibru@gmail.com, Sunita M <sunita3481@gmail.com>, prashardeepak99@yahoo.in, subhashis.ooty@gmail.com, "Dr. Anupom Borah" <anupomborah@gmail.com>, "N. Sree Harsha" <harsha1975@gmail.com>, vishal trivedi <vishaltrivediqa@gmail.com>, "SH. VINOD NAUTIYAL" <vnautiyal@gkv.ac.in>, "Dr.Mahadeva Rao" <raousm@gmail.com>, raousm@unisza.edu.my, dr_santosh@msu.edu.my, "Erwin M. Faller" <emfaller@ceu.edu.ph>, "skspharmacology@gmail.com" <skspharmacology@gmail.com>, soni_priyanka21@rediffmail.com, "jiyauddin_khan@msu.edu.my" <jiyauddin_khan@msu.edu.my>, uditaagrawal.phama@gmail.com, Andang MIATMOKO <andang-m@ff.unair.ac.id>, pharm.anas.alhamdany@uomustansiriyah.edu.iq, SRIJA SUR <sursrija0714@gmail.com>, vivek dave <attachvivek@gmail.com>, priya shrivastava <shrivastavap007@gmail.com>, abbma71@gmail.com, ABU MD ASHIF IKBAL <abumd97@gmail.com>

Dear Prof Ram,

Thank you very much. Here are a few corrections only as attached.

Erwin
[Quoted text hidden]
--

DR. ERWIN M. FALLER, RPh.,MSPharm.,MMPS.,FRIPharm.
Director, Internationalization and Linkage Office (InterLink),
Professor, Faculty of Pharmacy
San Pedro College, Philippines
H/P: (+63) 977 636 9421
Email: erwin_faller@spcdavao.edu.ph / erwinfaller1007@gmail.com

*****

Director, Center for Pharmacy Practice, Research and Policy
Chair, Institutional Biosafety Ethics Committee, San Pedro College, Philippines
Visiting Professor, Bournemouth University, United Kingdom
Editorial Board, Research in Social and Administrative Pharmacy (RSAP)